

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference WJW6250393/	FOR FURTHER ACTION	See item 4 below
International application No. PCT/GB2004/004153	International filing date (<i>day/month/year</i>) 27 September 2004 (27.09.2004)	Priority date (<i>day/month/year</i>) 29 September 2003 (29.09.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THE UNIVERSITY COURT OF THE UNIVERSITY OF ABERDEEN		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 03 April 2006 (03.04.2006)
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 12 JAN 2005

PCT WIPO PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/004153

International filing date (day/month/year)
27.09.2004

Priority date (day/month/year)
29.09.2003

International Patent Classification (IPC) or both national classification and IPC
C07B59/00, C07D279/20, A61K31/5415, A61P35/00

Applicant

THE UNIVERSITY COURT OF THE UNIVERSITY OF ABERDEEN

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004153

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004153

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004153

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 49,50,59-62

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 49,50,59-62
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004153

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-62
	No: Claims	
Inventive step (IS)	Yes: Claims	1-62
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-48,51-58
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Reference is made to the following documents:

- D1: TURNER J ET AL.: "Localization of carbon-11 radiopharmaceuticals in the Greene melanoma of hamsters" EUR. J. NUCL. MED., vol. 10, no. 9-10, 1985, pages 392-397, XP002312360
- D2: R. IWATA ET AL.: "A combined loop-SPE method for the automated preparation of [^{11}C]doxepin" J. LABEL. COMP. RADIOPHARM., vol. 45, 2002, pages 271-280, XP002312361

1. Novelty and Inventive Step (Article 33(2) and 33(3) PCT)

The present application fulfills the requirements of Article 33(2) and 33(3) PCT with respect to novelty and inventive step.

The present application deals with a method of [^{11}C]-labelling of phenothiazine and phenothiazine like compounds by reacting such compounds with [^{11}C]methyltrifluoromethanesulfonate thereby converting a pendant group comprising an amino or imino group into a corresponding [^{11}C]methyl labelled pendant group. The compounds are used in PET-imaging and in the treatment of melanomas and Alzheimer.

The closest prior art document is D1, which discloses on page 392 a method to [^{11}C]radiolabel chlorpromazine by reacting [^{11}C]formaldehyde with monodesmethyl derivative of chlorpromazine. The compound is used to localize tumours in hamsters using PET-scan.

The difference of the disclosure in document D1 and the present application is that in D1 a pendant amine group is converted using ^{11}C -formaldehyde whereas in the present application [^{11}C]methyltrifluoromethanesulfonate is used for this purpose. Therefore is the present application novel over the prior art.

Document D2 discloses in Scheme 1, the reaction of [^{11}C]methyltrifluoromethanesulfonate with nordoxepin, in which a pendant methylamine group is converted to a labelled [^{11}C]methyl-methylamine group and/or to a positively charged [^{11}C]dimethyl-methyliminium triflate. The difference of this disclosure and claim 1 of the present application is that in this disclosure nordoxepin is [^{11}C]radiolabelled, whereas in the present application a phenothiazine or phenothiazine like compound is [^{11}C]radiolabelled.

The problem to be solved by the applicant was to provide an alternative solution for [¹¹C]radiolabelling phenothiazine or phenothiazine like compounds. Starting from D1 a skilled person would not apply the knowledge of [¹¹C]radiolabelling using [¹¹C]methyl-trifluoromethanesulfonate as described in D2 on the compounds as described in D1 as there is no incentive in both documents to do so.

It is therefore considered that claim 1 and its dependent claims 2-45 are inventive over the prior art.

Claim 46 is about a compound obtained by a method according to the inventive process of claims 1-45. The compounds as disclosed in D1 are the closest prior art. These compounds are used for the same purpose. As the compounds are produced by an inventive process and because the compounds are a non-obvious alternative because of the inventive process, the compounds as claimed in claim 45 are considered inventive over the prior art.

Claims 47 and 48 deal with compositions comprising inventive compounds of claim 46. These claims are therefore also inventive.

Claims 49-62 are about the use of inventive compounds of claim 46 or inventive compositions of claims 47,48. These uses are inventive.

2. Acknowledgement of prior art (Rule 5.1(a)(ii) PCT)

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.